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EXAMINER	
ZHOU, SHUBO	

ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,062	BRUCE ET AL.	
	Examiner	Art Unit	
	SHUBO (Joe) ZHOU	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,21 and 38-56* is/are pending in the application.

4a) Of the above claim(s) *20,21,38-41 and 56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 February 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/18/05, 7/26/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Amendments

Applicants' election of Group III (claims 42-55) in the response filed 8/18/08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election **without** traverse (MPEP § 818.03(a)).

Claims 20-21, and 38-56 are presently pending, where claims 20-21, 38-41 and 56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 42-55 are under consideration.

Sequence Rules Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). Such sequences are present at least on page 45 of the specification and in Figure 6. However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because the sequences are not followed by a sequence identifier. Applicants are reminded that it is required that a sequence identifier (SEQ ID NO:X) be amended into the specification at each sequence, and that when a sequence is presented in a drawing regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier must be used, either in the drawing or in the Brief

Description of the Drawings. Failure to comply with these requirements may result in ABANDONMENT of the application under 37 CFR 1.821(g). Applicants are given the same response time regarding this failure to comply as that set forth to respond to this office action including providing a paper copy, a computer readable form of a Sequence Listing containing this sequence, and a statement under 37 CFR 1.821(f).

Drawings

The drawings filed 2/18/05 are objected to because at least parts of figures 1-2 and 6-8 are not legible. Accordingly, replacement drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to this Office action. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures.

Specification

The specification is objected to because of the following including informalities:

Trademarks are used in this application, such as GENBANK™ on page 48. All trademarks should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort should be made to prevent their use in any manner that might adversely affect their validity as trademarks.

The disclosure is objected to also because it contains an embedded hyperlink and/or other form or browser-executable code. Such code is present in the specification at least on page 15. Applicants are required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP ' 608.01.

Appropriate correction is required.

Claim Rejections-35 USC § 112

The following is a quotation of the **second** paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 42-55 are rejected under 35 U.S.C. 112 , second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 42 recites "mutagenizing a Staphylococcus genome with a transposon such that individual cells containing at least on transposon insertion are isolated." The limitation is confusing because of the phrase "individual cells containing at least on transposon insertion are isolated." Is "at least one transposon insertion" intended?

Claim 42 also recites "collecting and mapping said at least one transposon insertion in each individual cell so as to form a database of transposon insertion sites, or an HTTIM." The metes and bounds of the claim are not clear because it is unclear as to what is meant by the "collecting" step and it is unclear as to exactly what is being collected. Are cells containing

transposons are collected or literally as indicated in the claim, a transposon insertion is collected, which is also unclear because it is not clear how an insertion, which is an event, is collected. Or is the transposon insert itself is collected? Furthermore, the phrase "said at least one transposon insertion" lacks clear antecedent basis as there is no prior reference in the claim to at least one transposon insertion.

The phrase "said bacteria" recited in claim 43 lacks sufficient antecedent basis because there is no prior reference to bacteria.

Claim 45 recites "wherein said transposon is 3000 to 6000." It is unclear what is meant by the phrase, the transposon is 3000 to 6000 base pairs long or there are 3000 to 6000 transposons in a cell, or else.

Claim 52 recites "comprising the statistical method applied herein." The metes and bounds of the claimed invention are not clear because it is unclear what is meant by "herein."

Clarification of the metes and bounds of the claims is requested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 42-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Charles et al. (IDS document: WO 01/07651 A2, 1 February 2001) in view of Haselbeck et al. (IDS document: WO 01/70955 A2, 27 September 2001).

In view of the indefiniteness of the claims as set forth above, the references cited are being applied to the best interpretation of the claims as currently written.

The claims are drawn to a method for identifying a library of putative essential or important genes using a High Throughput Transposon Insertion Database (HTTIM), comprising: a) mutagenizing a Staphylococcus genome with a transposon such that individual cells containing at least on[e] transposon insertion are isolated;

b) collecting and mapping said at least one transposon insertion in each individual cell so as to form a database of transposon insertion sites, or an HTTIM;

c) comparing said database of transposon insertion sites with a database comprising the genomic sequence of the bacterium to identify open reading frames in said genomic sequence database that are not disrupted by a transposon insertion; and

d) forming a library from said putative essential or important genes that are not disrupted by a transposon.

Charles et al. disclose a method for making a library of putative essential genes comprising mutagenizing bacterial cells such as Staphylococcus genome with transposon to obtain a library of mutants; and isolating polynucleotide sequences from the library which flank the inserted transposon sites to obtain a pool of consensus probes. These steps are interpreted as the "mutagenizing" and the "collecting" steps recited in the instant claims. The method of Charles et al. also includes hybridizing the consensus probes with a polynucleotide library from the same organism, and identifying nucleotide sequences in the library to which the consensus probe sequences do not hybridize, which are putative essential genes of the organism. See at least pages 2 and 6-7. Since the consensus sequences are those flanking the transposons, they represent those genes that are disrupted by the transposons. Those sequences from the library that are identified as not being hybridized to the consensus sequences are those genes that are not disrupted by any transposons. Charles et al. also disclose that ideally the hybridization is done with the library in the form of a gridded array that represents the whole genome of the organism and each location represents a single open reading frame. When the entire genomic sequence is known, the order of all the open reading frames is known and the transposon sites are thus

mapped by the hybridization. See at least pages 13-14. This hybridization step is interpreted as comparing a pool of sequences of the insertion sites (interpreted as a file of sequences of insertion sites) with a library of genomic sequences of the organism.

Charles et al. do not explicitly disclose comparing a database of transposon insertion sites with a database comprising the genomic sequence of the organism. However, Charles et al. do teach the use of bioinformatics tools to allow rapid isolation of further essential genes by searching databases of known genomic sequences to isolate orthologous genes, etc. See page 17.

Haselbeck et al. disclose a method for identifying putative essential genes by using antisense sequences. The method comprises identifying nucleotide sequences from the inserts of vectors that represent sequences of genes affecting proliferation and growth, comparing the sequences with know genomic sequences of the organism in databases such as GenBank, TIGR databases and the Pathoseq database to identify open reading frames that comprise these sequences, which are genes affecting proliferation and growth. See at least pages 94-96.

It would have been obvious to one of ordinary skill in the art at the time of the invention that the way of comparing isolated sequences with known databases containing entire genomic sequences and/or all open reading frames to identify genes or open reading frames as disclosed by Haselbeck et al., would be much more advantageous, such as time saving, than the physical hybridization method as disclosed by Charles et al. Therefore, one of ordinary skill in the art at the time of the instant invention was made would have been motivated to modify the method of Charles et al. to applying the method of comparing a database of sequences of insertion sites with a database containing the entire genomic sequence and all the open reading frames of the organism to take advantage of the latter method such as to save time.

With regard to claims 45-50 which specify the approximate numbers of transposons in the mutant library and number of genes in the library of putative essential genes, it would have been obvious to one of ordinary skill in the art that the number of transposons in the mutant library and the number of essential genes as disclosed by Charles would vary depending on the scale and exhaustiveness of the particular experiment and the genome size of the organisms up to the maximum number of essential genes. Charles et al. encourage combining two transposon libraries thereby increasing the probability of obtaining transposon insertions in a greater number of genes. See page 9.

With regard to claims 51-52, which recite statistical calculations, given that Charles et al. and Haselbeck et al. teach of using bioinformatics tools including searching databases of GenBank etc. using BLAST and database comparison, it would have been readily apparent that certain statistical calculations such as probability would be applied.

With regard to claims 53-55, which recite verifying the essential genes, Charles et al. disclose a method of such verification involving creating promoter swap mutants. See pages 16-17.

Special Notes from the Examiner

The method claims are interpreted to have a physical transformation because the steps of "mutagenizing" and "collecting" are construed as physical steps of inserting transposons into the genome by an experimental procedure that transformed at least a bacterial genome without the transposon into a genome with the transposon inserted into various sites therein, and it is construed that no embodiment of the claimed invention includes an in silico step of

"mutagenizing" and "collecting." Because of this, no rejection under 35 USC 101 (patent subject matter eligibility) is made.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran, can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Shubo (Joe) Zhou/

SHUBO (JOE) ZHOU, PH.D.

PRIMARY EXAMINER